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To Examiner : Alstrum Acevedo, James Henry

Group 1616

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Docket No. 2685.2046 US3
Expedited Procedure under 37 C.F.R. 1.116
Examining Group 1616

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellants: Richard P. Batycky, Giovanni Caponetti, Mariko Childs, Elliot Ehrich, Karen Fu, Jeffrey S. Hrkach, Wen-I Li, Michael M. Lipp, Mei-Ling Pan and Jason Summa

Application No: 10/607,571 Group No: 1616

Filed: June 26, 2003 Examiner: James Henry Alstrum Acevedo

Confirmation No.: 6287

Title: Inhalable Epinephrine

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APPEAL BRIEF

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Sir:

This Brief is being filed pursuant to 37 CFR 41.37. The fee under 37 CFR 41.20(b)(2) was paid on November 9, 2006. No additional fee is believed to be due. The required sections under 37 CFR 41.37 are set forth below under separate headings.

(1) The Real Party of Interest

The real part of interest in this appeal is Advanced Inhalation Research by virtue of the Assignment recorded on September 19, 2003 at Reel 015310 and Frame 870.

(2) Related Appeals and Interferences

There are no related appeals or interferences at this time known to the appellant, the assignee or its representative which will directly affect or be directly affected by or have a bearing in the Board's decision in the pending appeal.

(3) Status of the Claims

Claims 140-144, 146-150, 153, and 156-173 are pending and finally rejected. **Claims 140-144, 146-150, 153, 156-170, 172 and 173 are appealed.** Claims 1-139, 145, 151, 152, 154 and 155 have been canceled. No claims are withdrawn from consideration.

(4) Status of the Amendments

An Amendment after Final was filed on July 6, 2006. The amendment has been entered as per the Decision on Petition dated January 8, 2007.

(5) Summary of Claimed Subject Matter

Appealed claim 140 is directed to a method of administering spray-dried particles of epinephrine and a pharmaceutically acceptable excipient to the respiratory system of a patient via inhalation wherein the particles comprise at least about 50 micrograms of epinephrine and are administered in a single inhalation and wherein the particles have a tap density of less than 0.4 g/cm^3 and posses a fine particle fraction of less than 5.6 microns of at least 45%. Support for the claim is found on page 4, lines 18-25; page 6, line 29 to page 7, line 4 (spray dried particles); page 31, lines 8-15 (low tap density); page 56, lines 2-7 (dose). Claim 140, as amended in the Amendment after final, contains the claim limitations found in Claims 151, 152, 154, and 155.

Appealed claim 172 is an independent claim and is directed to particles for delivery of epinephrine to the respiratory system comprising: (a) about 11 to about 21 weight percent epinephrine bitartrate; (b) about 62 to about 82 weight percent leucine; and (c) about 7 to about 17 weight percent sodium tartrate. This claim is supported on page 6, lines 16-28.

Appealed claim 173 is an independent claim and is directed to methods of treating a patient in need of epinephrine by administering an effective amount of particles to the respiratory system of the patient, the particles comprising: (a) about 11 to about 21 weight percent epinephrine bitartrate; (b) about 62 to about 82 weight percent leucine; and (c) about 7 to about 17 weight percent sodium tartrate. This claim is supported on page 6, lines 16-28.

(6) Grounds of Rejection to be Reviewed on Appeal

- That the Examiner has failed to show that claims 140-144, 154 and 156-160 are anticipated by Tarara (US 2005/0074498) hereinafter referred to as "Tarara".
- That the Examiner has failed to show that claims 152, 153 and 155 (which collectively correspond to Claim 140, as amended) are obvious under 35 U.S.C. §103(a) over Tarara et al.
- That the Examiner has failed to show that claims 161-162 are obvious under 35 U.S.C. §103(a) over Tarara et al. in view of the 56th edition (2002) of the Physician's Desk Reference (hereinafter the "PDR").
- That the Examiner has failed to show that claims 140-143, 146-151, 159, 160 and 162 are obvious under 35 U.S.C. §103(a) over Foster (US 2003/0215512) hereinafter referred to as "Foster", in view of Tarara.
- That the Examiner has failed to show that claims 163-170 are obvious under 35 USC 103(a) as being unpatentable over Tarara in view of Warren (Clin. Pharmacol. Ther., 1986, 40(6), 673-678; "Warren").
- That the Examiner has failed to show that claims 140-143, 146-151, 159, 160 and 162 are unpatentable under 35 U.S.C. §103(a) over Foster (US 2003/0215512) hereinafter referred to as "Foster", in view of Tarara, and further in view of the Drug Information Handbook (DIH).

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(7) Argument

I. Rejection of Claims 140-144, 154 and 156-160 under 35 U.S.C. §102(e) over Tarara.

The Examiner has finally rejected Claims 140-144, 154 and 156-160 under 35 U.S.C. §102(e) over Tarara. Claim 140 has been amended to include the limitations of Claims 151, 152, 154, and 155. Claims 141-144, 156-160 depend from Claim 140. Claim 154 has been canceled. Insofar as Claims 151, 152 and 155 have not been rejected on this ground and all of the limitations of these claims have been inserted into Claim 140, it is believed self-evident that the rejection should be withdrawn or reversed.

II. Rejection of Claims 152-153 and 155 under 35 U.S.C. §103(a) over Tarara

Claims 152, 154 and 155 have been canceled and Claim 140 has been amended to include the limitations. Thus, it is believed that this rejection is believed to be relevant to Claim 140 and the claims which depend therefrom.

In the Final Office Action, the Examiner states that Tarara does not anticipate claims 152, 153 and 155 because Tarara does not expressly teach the dosage amounts recited in the claims administered in a single inhalation. The Examiner asserts that Tarara implicitly teaches administration of particles comprising epinephrine in a single inhalation because Tarara teaches that a unit dose container in a DPI may contain from 5 to 15 mg of dry powder, corresponding to a drug loading range from 25 to 500 micrograms per dose. The Examiner further asserts that one dose comprises a single inhalation because the actuation step in the use of a dry powder requires a patient to inhale the medical composition from the DPI. The Examiner is incorrect.

A. Claim 140

The Examiner has provided no basis for concluding that a generic teaching that a unit dose container in a DPI which may contain from 5 to 15 mg of dry powder, whether or not it contains a drug load of 25-500 micrograms, teaches the desirability and means to deliver at least 50 micrograms of epinephrine to a patient in need thereof in a single breath. The actual dose per actuation (as compared to breath) will depend upon a variety

of factors such as the amounts of active agent and the excipients, the product morphology, and the inhaler used. Further, it is not clear where the Examiner has any basis for asserting that each actuation of any inhaler corresponds to a single breath. The Examiner has also provided no evidence that it would be obvious from Tarara to deliver at least 50 micrograms of any drug, including epinephrine, to a patient in a single inhalation.

To review the specific reference teachings, in Example XXI, for example, Tarara states that the beclomethasone diproprionate (BDP) powder dose delivered to the relevant stages of the cascade impactor is "77 micrograms per actuation". See, paragraph 0318 of Tarara. However, in paragraph 0315, Tarara states that there were twenty actuations. Thus if 300 micrograms of spray dried microspheres were loaded into the inhalation device as stated by Tarara in paragraph 0314, it is not possible that the delivered dose was 77 micrograms per actuation as 77 micrograms per actuation multiplied by 20 actuations would far exceed the total number of micrograms of spray-dried powder initially loaded into the inhaler for delivery. Likewise, if 100% of the drug was delivered over 20 actuations, the average amount of drug per actuation could not exceed 50 micrograms. Further, even if 77 (or 100) micrograms of drug were delivered in a single actuation out of the 300 micrograms loaded into the inhaler, an FPF of at least 45% for that actuation was not achieved. Clearly, something is wrong with the data provided in Tarara's examples on its face. Further, the inhaler (DPI) used is only described as being "proprietary," relying upon the use of a HFA propellant to actuate the dose. It is not clear that the inhaler permits each actuation to be inhaled in a single breath or is a breath activated inhaler. It is impossible to tell from the data presented in Tarara whether at least 50 micrograms of BDP or for that matter, any other drug including epinephrine, can be delivered in a single, breath-activated step.

During the interview of July 6, 2006, the Examiner pointed to a disclosure in Tarara which states "[c]urrently, bulk reservoir type DPIs can meter between 200 micrograms and 20 mg powder per actuation". The Examiner asserted that this statement was a teaching that a powder is delivered to the patient within the presently claimed dosage range in a single, breath-activated step. This is not the case. A bulk reservoir DPI that can actuate between 200 micrograms and 20 mg of powder per actuation is not

equivalent to 50 micrograms of powder *delivered* to the patient in a single, breath-actuated step. As defined in the application, the term "single, breath-actuated step" means that the particles are dispersed and inhaled in one step wherein the energy for the dispersion is provided by the patient. See, page 57, lines 6-24 of the present specification. Examples of suitable, single, breath activated inhalation devices are listed on page 57, lines 14-21 of the present specification. Bulk reservoir type DPI inhalers generally rely on additional energy other than the energy supplied by the patient's breath. U.S. Patents 5,458,135 and 5,997,848, owned by the same assignee as Tarara, disclose such inhalers (Exhibits A and B). The device described in U.S. Patent 5,458,135 takes dry powder from a powder reservoir and draws it into an air stream using a dispersion nozzle. Even though the patient *may* inhale the entire dosage in a single breath, this procedure is not the same as a single-breath activated step as defined in the present specification.

The Examiner also relies upon Para [0132] for teaching drug loading and dose. However, like Example XXI, the numbers in the paragraphs do not appear to work. The inhaler is said to be loaded with 5 to 15 mg of product, which "corresponds to a drug loading ... of 25 to 500 μg per dose." The preferred products possess at least 50% weight active agent. Para. [0068]. Thus, in a 15 mg product, *at least* 7.5 mg is active agent in a *preferred* embodiment. If one assumes the *maximum* 500 μg dose is achieved with the *lowest* value of the preferred range (7.5 mg drug) and the word "dose" refers to the amount of drug delivered (irrespective of the number of actuations required to deliver the drug) then the respirable portion (e.g, fine particle fraction of the emitted dose) of the product (500 μg dose out of 7.5 mg drug that is deliverable to the patient) must be *no more* than about 7%, far less than the present claim which requires a fine particle fraction of at least 45%. If one instead assumes the 500 μg to be the amount of active agent in the inhaler of the 15 mg of product (rather than the delivered dose), the drug load is only about 3.3%, well *below* the preferred ranges in Para. [0068]. In this interpretation of the teachings, the *highest* drug load taught is 10% (500 μg of 5 mg), again *far below* the most preferred ranges. It is true that the patent specification teaches a large number of ranges (drug load, fine particle fraction, amount of drug actuated, dose delivered, inhaler selection and operation) which values or parameters can be identified and individually

selected to theoretically achieve the claimed combination. However, as established by comparing a very few of the ranges above, these numbers are not internally consistent but appear to be arbitrary. It is respectfully asserted that such teachings of what is "preferred" cannot be said to provide any meaningful guidance that renders the claimed selection obvious.

Even if Tarara were held to teach all of the individual components of the present claims, there is no teaching or suggestion that would motivate or lead one skilled in the art to select the specific combination or the specific delivered doses, in a single inhalation or breath activated step and fine particle fractions of the present claims.

To establish a *prima facie* case of obviousness, there must be a reasonable likelihood of success for a claimed combination. *In re Vaeck*, 947 F.2d 488, 20 USPQ 2d 1438 (Fed. Cir. 1991). Additionally, a reference that generically describes various elements of the claims does not *per se* establish that the claims are obvious under 35 U.S.C. 103. See *In re Baird*, 16 F.3d 380, 382; 29 USPQ2d 1550 (CCPA 1979). The Examiner has not provided any motivation as to why one skilled in the art would combine epinephrine (mentioned in a long list in Tarara), with a single, inhalation and expect to deliver with high efficiency, 50 micrograms (as claimed in claim 152), of epinephrine to a patient who is in need of epinephrine, and, thereby is likely to be in severe respiratory distress. Tarara does not even teach highly efficient administration of drugs (products having an FPF of at least 45% in a single breath) to normal healthy patients. As explained above, Example XX appears to state that ten (not one) actuations of the inhaler containing 300 micrograms of product were made. The DPI actuation was not breath actuated but produced with a fluorocarbon propellant. No one actuation appeared to achieve an FPF of at least 45%. Example XXI appears to state that twenty (not one) actuations of the inhaler containing 300 micrograms of product were made. Again, the DPI actuation was not breath actuated but produced with a fluorocarbon propellant. No one actuation appeared to achieve an FPF of at least 45%. The Examiner has offered no technical reason to believe that substantially better results would be expected with a similar product containing epinephrine and a DPI that was actuated once (versus ten or twenty times) without the assistance of an HFA propellant. The Examiner

has not met his burden in establishing that the person of ordinary skill in the art would be motivated to administer, with high efficiency, epinephrine to a patient in need thereof.

Likewise, with respect to the limitation that the administration be achieved in a single breath, the Examiner has not provided any motivation as to why one skilled in the art would combine epinephrine (mentioned in a long list in Tarara), with delivery via a breath activated inhaler in a single breath-activated step and yet deliver with the claimed high (as claimed in claim 155), despite the patient's likely severe respiratory distress. It is noted that DPIs of any type were viewed in the art to have many drawbacks related to their reliance on inspired air from the patient. See for example column 1, lines 51-57 of Exhibit A (U.S. Patent No. 5, 458,135) where the many disadvantages of DPI's are described. Without the benefit of hindsight in view of the present invention, one skilled in the art would not be motivated to rely on a breath-actuated dry powder inhaler to deliver a life saving drug in a crisis situation that also involved difficulty in breathing. At best, if one were to attempt delivering epinephrine to a patient according to the teachings of Tarara, one would select the preferred MDIs or bulk reservoir DPIs. Even in this embodiment, one would not necessarily expect that the efficiency of delivery to be so high. Yet, as disclosed in the present examples page 92, lines 8-16, T_{max} and C_{max} were *superior* to injection using the EpiPen® and standard IM injection. Given the teachings in the art that would discourage administering such drugs with these inhalers, this is a truly unexpected result.

In view of the above discussion, withdrawal of the rejection is respectfully requested.

III. Rejection of Claims 161-162 under 35 U.S.C. §103(a) over Tarara et al. in view of the 56th edition (2002) of the Physician's Desk Reference (hereinafter the "PDR").

The Claims depend from Claim 140 and further define the patient to be treated (i.e., a patient suffering from anaphylaxis (Claim 161) and a patient suffering bronchoconstriction, bronchospasm, airway constriction, or edema (Claim 162)). Tarara is relied upon as above. The PDR is relied upon to show that epinephrine is known to treat these diseases.

While it is not disputed that the PDR establishes that epinephrine is known to treat these diseases, it is not conceded that it would be obvious to treat these kinds of diseases by pulmonary delivery of the product that is described above in Claim 140. Given the high efficencies in delivery and the large cloud that will result from the actuation of a highly efficient and large dose, it is not at all obvious to treat a patient suffering from anaphylaxis (Claim 161) and a patient suffering bronchoconstriction, bronchospasm, airway constriction, or edema (Claim 162). The fact that the PDR suggests that the drug is known to be administered for a given disease does not necessarily support a conclusion that any and all modes of administration of that drug would be obvious.

IV. Rejection of Claims 140-143, 146-151, 159-160 and 162 under 35 U.S.C. §103(a) over Foster in view of Tarara

Claim 140 has been amended to include the limitations of Claims 151, 152, 154, and 155. Claims 141-144, 156-160 depend from Claim 140. Claim 154 has been canceled. Insofar as Claims 151, 152 and 155 have not been rejected on this ground and all of the limitations of these claims have been inserted into Claim 140, it is believed self-evident that the rejection should be withdrawn or reversed.

V. Rejection of Claim 163-170 under 35 U.S.C. §103(a) over Tarara in view of Warren

Tarara is relied upon by the Examiner as above. Likewise, for all the reasons set forth above, Tarara does not teach the claim limitations of Claim 140, the claim from which claims 163-170 depend.

It is stated that Tarara lacks the express teaching of Cmax and Tmax of different administration routes. The reference relies upon Warren to show that inhalation of 30 puffs (i.e., not in a single breath) of adrenaline from a pressurized aerosol (not a breath actuated dry powder inhaler) are comparable to those achieved by a subcutaneous injection. Nor does Warren teach that it would be obvious to administer epinephrine by a breath actuated dry powder inhaler. The inhaler of Warren relies upon the external energy of a propellant to disperse the drug and then a large number of breaths to deliver

the drug. It is believed that the amendment to the claims to include the limitations of Claims 151, 152, 154 and 155 avoid the rejection as the secondary reference provides no substantive teachings that an effective dose of epinephrine can be achieved in a single breath actuated administration from a dry powder inhaler.

VI. Rejection of 172 and 173 under 35 U.S.C. §103(a) as being unpatentable over Foster in view of Tarara and further in view of the Drug Information Handbook ("DIH")

The claims are directed to a very specific formulation of epinephrine bitartrate, leucine and sodium tartrate and their use in treating patients. The Examiner finds the formulations and method obvious. Appellants disagree.

The Examiner states that the use of epinephrine bitartrate would have been apparent to a skilled artisan because it is "one of the most common salts of epinephrine employed in pharmaceutical formulations." The Examiner relies upon Foster to teach adding a glass former, such as tartrate, and an additional excipient such as leucine in the formulation. Regarding the amounts of each ingredient, the Examiner asserts that the teaching in Foster of a range of 0.05% to 99.0% active agent makes obvious the selection of 11 to 21% epinephrine bitartrate and, with respect to the remaining excipients, it is a parameter that is routinely optimized.

To establish a *prima facie* case of obviousness, the prior art reference (or references when combined) must teach or suggest all of the claim limitations. There must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. There must also be a reasonable expectation of success. *See* M.P.E.P. §§2143. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in Appellant's disclosure. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). Thus, "particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed inventions, would have selected these components for combination in the manner claimed." *In re Kotzab*, 217 F.3d 1365, 1371 (Fed. Cir. 2000). "The factual inquiry whether to combine references must be thorough and searching. It must be based on objective evidence of record. This precedent has been reinforced in myriad decisions,

and cannot be dispensed with." *In re Sang Su Lee*, 277 F.3d 1338, 1343 (Fed. Cir. 2002) (citations and quotes omitted). Additionally, it is now well-established that "[b]road conclusory statements regarding the teaching of multiple references standing alone are not 'evidence'." *In re Kotzab*, 217 F.3d at 1370. "Th[e] factual question of motivation is material to patentability and [can] not be resolved on subjective belief and unknown authority." *In re Sang Su Lee*, 277 F.3d at 1343-44.

While both Foster and Tarara mention adrenaline (epinephrine) as part of a long list of actives, the mere fact that both references disclose overlapping lists of active agents for incorporation of particles does not provide the skilled practitioner with an expectation of successfully mixing and matching specific excipients and active agents in specific amounts. Neither reference discloses or suggests the desirability of producing the specific epinephrine formulation as claimed in claims 172 and 173 nor has the Examiner provided any evidence that would motivate the skilled practitioner to combine the teachings of Foster and Tarara in order to prepare epinephrine containing particles. The Examiner has merely concluded that because both references mention both "particles" and "adrenaline" that they should be combined. This is improper.

The specific formulations are not reasonably taught by Foster, the primary reference, alone or when combined with Tarara and the DIH. Foster teaches a nearly infinite number of possible combinations of a large number of active agents and a large number of excipients. There is no guidance within this broad generic disclosure to couple epinephrine bitartrate, leucine and sodium tartrate in the specific amounts claimed.

The preferred active agents of Foster appear to be proteins, polypeptides and other macromolecules. Although small molecule drugs are also described and may be "adrenalin," specific salts thereof are not disclosed. It is noted that salts of many drugs are described in the same list. Had Foster intended to teach salts of epinephrine, he would have. With respect to the amount of active agent added, the reference's range of 0.05% to 99.0% by weight of active agent is, essentially meaningless because it spans the entire range of possible amounts. That is, it is difficult to imagine a therapeutically effective product where the amount of active agent is substantially lower than 0.05%. Further, since Foster appears to rely upon the formation of a glassy matrix and since the

Examiner has not shown that epinephrine would be expected to be glassy, it is not clear that Foster teaches a 99.0 or 100% epinephrine formulation. In any event, a range of essentially no active agent to essentially all active agents is not a meaningful teaching of any particular amount of drug to add. The preferred range of between 0.2% and 97% is hardly more meaningful. Para. [0054]. Such a range hardly suggests to the person of skill in the art to select the range between 11 and 21%. The only small molecule working examples carried less than 5% drug. See Example 16.

The excipients of Foster span several columns. The Examiner relies upon the teaching of adding a "glass former" to suggest that sodium tartrate can be added. In fact, the reference suggests that any glass former can be used and, where the drug itself forms a glass, can be omitted altogether. Para. [0064]. Sodium tartrate is one of several glass formers that could be used, in addition to peptides, carbohydrates such as mannitol (when used in combination with, for example, glycine) or lactose, citric acid and sodium citrate. Sodium citrate was the structurally closest glass former actually used. However, it appears that all of the working examples employed large amounts of glass formers, in various combinations. There is no guidance to select between about 7 and 17% of this particular compound. There is no suggestion that this particular combination would be expected to result in a glassy matrix.

Furthermore, the claims require the addition of a large amount of leucine. Leucine is not disclosed as a preferred excipient (or "additive") and there is no guidance in this reference which would suggest that it would be desirable to select leucine and add it in a large quantity. The amount of any one excipient is also not described in a meaningful way to suggest a preferred amount as the teachings are limited to 3% to 99.8% by weight [Para. [0079]]. In fact, this passage suggests that such "additives" should be added in an amount less than 20% w/w. The claims require the leucine to be added in an amount between about 62 and 82%. The reference simply provides no motivation to add such a substantial amount of leucine.

Turning to the working examples for meaningful guidance, 66.2% mannitol, 13.1% sodium citrate and 0.7% citric acid was used with 20% zinc-insulin in Example 1; 18.2% mannitol, 59.1% sodium citrate, 0.1% citric acid and 2.6% glycine was used with 20% zinc-insulin in Example 2; 10.1% mannitol, 27.1% sodium citrate, 0.2% sodium ion

and 2.6% glycine was used with 60% zinc-insulin in Example 3; 18.3% mannitol, 19.0% sodium citrate, 0.2% sodium ion and 2.6% glycine was used with 60% zinc-insulin in Example 4; 77.3% sodium citrate, 0.1% citric acid and 2.6% glycine was used with 20% zinc-insulin in Example 5; and so on. Not one example employs an amino acid at high concentrations; not one example employs either leucine or sodium tartrate; not one example employs epinephrine, much less epinephrine bitartrate. A sugar is present in almost every working example. The vast majority of the working examples formulate a protein or peptide. Albuterol sulfate, the only small molecule exemplified, was formulated with 95% or 98% lactose. There is simply no motivation in this exceedingly broad disclosure of a nearly infinite number of possible combinations to select the specific excipients of the claims, in the specific amounts and combine them with epinephrine.

More is required to support a *prima facie* case of obviousness than the mere fact that the words of the claim can be found within reference and the unsupported assertion that the rest that is missing from the reference is mere routine optimization. See *In re Baird*, 16 F.3d 380, 382; 29 USPQ2d 1550 (CCPA 1979).

The Conclusion

As the Examiner has failed to establish a prima facie case of obviousness and the unexpected results achieved by the present invention, Appellants request reversal of the rejection and allowance of the application.

Respectfully submitted,
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Dated: 1/23/07

(8) Claims Appendix

140. A method for treating a patient in need of epinephrine, the method comprising:

administering spray-dried particles from a dry powder inhaler to the respiratory system of the patient in a single, breath-activated step, the particles comprising:

(a) epinephrine, or a salt thereof; and

(b) at least one pharmaceutically acceptable excipient;

wherein the particles administered to the patient comprise at least about 50 micrograms of epinephrine, have a tap density of less than 0.4 g/cm^3 and possess a fine particle fraction of less than 5.6 microns of at least about 45 percent.

141. The method of Claim 140, wherein the epinephrine, or salt thereof, is present in the particles in an amount ranging from about 1 to about 95 weight percent.

142. The method of Claim 141, wherein the epinephrine, or salt thereof, is present in the particles in an amount ranging from about 1 to about 45 weight percent.

143. The method of Claim 142, wherein the epinephrine, or salt thereof, is present in the particles in an amount ranging from about 1 to about 30 weight percent.

144. The method of Claim 140, wherein the particles are aerodynamically light.

146. The method of Claim 140, wherein the particles are amorphous.

147. The method of Claim 140, wherein the epinephrine, or salt thereof, contained in the particles is amorphous.

148. The method of Claim 140, wherein the epinephrine, or salt thereof, contained in the particles is crystalline.

149. The method of Claim 140, wherein the pharmaceutically acceptable excipient contained in the particles is amorphous.

150. The method of Claim 140, wherein the pharmaceutically acceptable excipient contained in the particles is crystalline.

153. The method of Claim 140, wherein the particles comprise about 250 micrograms to about 5 milligrams of epinephrine.

156. The method of Claim 140, wherein a first portion of the particles is deposited in the airways of the respiratory system and a second portion of the particles is deposited to the alveoli region of the lungs.

157. The method of Claim 140, wherein administering an effective amount of particles includes delivering a portion of the particles to the alveoli region of the lungs.

158. The method of Claim 140, wherein administering an effective amount of particles includes delivering a portion of the particles to the upper airways.

159. The method of Claim 140, wherein the epinephrine is released from the particles and acts systemically.

160. The method of Claim 140, wherein the epinephrine is released from the particles and acts locally.

161. The method of Claim 140, wherein the patient in need of epinephrine is suffering from anaphylaxis.

162. The method of Claim 140, wherein the patient in need of epinephrine exhibits at least one of the conditions selected from the group consisting of bronchoconstriction, bronchospasm, airway constriction, and edema.

163. The method of Claim 140, wherein the coefficient of variation for the maximum epinephrine concentration, C_{MAX}, in the patient's blood plasma of a dose of epinephrine is lower than for a non-intravenous injection of the same dose of epinephrine.

164. The method of Claim 163, wherein the non-intravenous injection is selected from the group consisting of a subcutaneous injection, an intramuscular injection, and an auto-injection.

165. The method of Claim 140, wherein the coefficient of variation for the time for maximum epinephrine concentration, T_{MAX}, in the patient's blood plasma of a dose of epinephrine is lower than for a non-intravenous injection of the same dose of epinephrine.

166. The method of Claim 165, wherein the non-intravenous injection is selected from the group consisting of a subcutaneous injection, an intramuscular injection, and an auto-injection.

167. The method of Claim 140, wherein the average time for maximum epinephrine concentration, T_{MAX}, in the patient's blood plasma of a dose of epinephrine is lower than for a non-intravenous injection of the same dose of epinephrine.

168. The method of Claim 165, wherein the non-intravenous injection is selected from the group consisting of a subcutaneous injection, an intramuscular injection, and an auto-injection.

169. The method of Claim 140, wherein the median time to maximum epinephrine concentration, T_{MAX}, in the patient's blood plasma is less than about 5 minutes.

170. The method of Claim 140, wherein the resulting epinephrine C_{MAX} in the patient's blood plasma is about 2 to about 3 times greater than epinephrine C_{MAX} in the patient's blood plasma provided by administration of a liquid-based aerosol.

172. Particles for delivery of epinephrine to the respiratory system, the particles comprising:

(a) about 11 to about 21 weight percent epinephrine bitartrate;

(b) about 62 to about 82 weight percent leucine; and

(c) about 7 to about 17 weight percent sodium tartrate.

173. A method for treating a patient in need of epinephrine, the method comprising:

administering an effective amount of particles to the respiratory system of a patient using a dry powder inhaler, the particles comprising:

(a) about 11 to about 21 weight percent epinephrine bitartrate;

(b) about 62 to about 82 weight percent leucine; and

(c) about 7 to about 17 weight percent sodium tartrate.

(9) Evidence Appendix

NONE

(10) Related Proceedings Appendix

NONE